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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,840	01/31/2001	Brian P. Dwyer	257/245	2714

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MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
TRAN, MY CHAU T	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/775,840	DWYER ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/12/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-113* is/are pending in the application.

4a) Of the above claim(s) *1-40,42,43,45-48,53,58,61,63,67-70 and 72-113* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41,44, 49-52, 54-57, 59-60, 62, 64-66, and 71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3, 9, & 13*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-113 are pending.

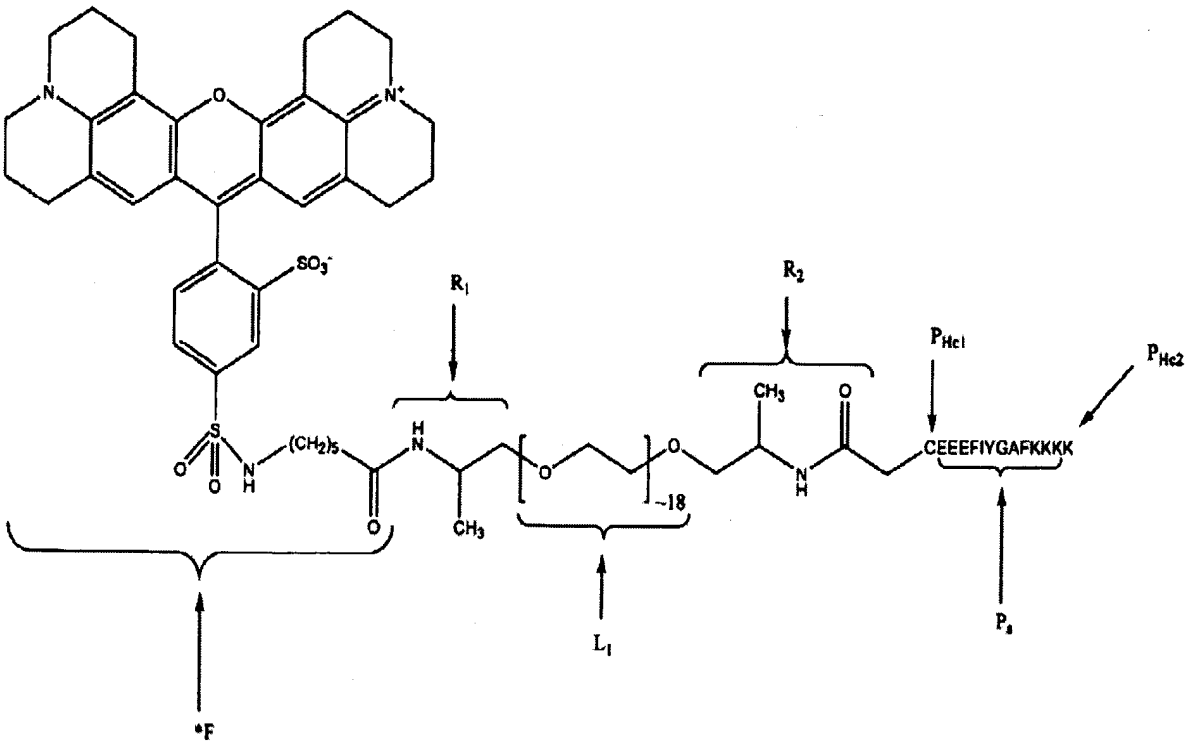
Election/Restrictions

2. Applicant's election of traverse of Group VII (Claims 41, 43-52, and 54-77; drawn to a library of water-soluble pegylated kinase substrate) in Paper filed 3/12/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 1-40, 42, 53, and 78-113 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to ***nonelected inventions***, there being no allowable generic or linking claim. Election was made **without** traverse in Paper filed 3/12/04.

4. Applicant has elected the following species for the elected invention (Claims 41, 43-52, and 54-77; drawn to a library of water-soluble pegylated kinase substrate):

a. The elected species of a library of water-soluble pegylated kinase substrate that would read on the formula of $*F\text{-}R_1\text{-}L_1\text{-}R_2\text{-}P_{Hc1}\text{-}P_S\text{-}P_{Hc2}\text{-}(R_3\text{-}L_2\text{-}R_4\text{-}T)_y$ is



For the portion $(R_3\text{-}L_2\text{-}R_4\text{-}T)_y$, y = 0; therefore $(R_3\text{-}L_2\text{-}R_4\text{-}T)$ is removed.

Note: the elected species is disclosed in the specification of page 34 (scheme 2), which is Texas Red-Jeffamine$_{900}$-CEEEFIYGAFKKKK [SEQ. ID. No. 1]. Furthermore, it is noted that "[F]or the portion $(R_3\text{-}L_2\text{-}R_4\text{-}T)_y$, y = 0; therefore $(R_3\text{-}L_2\text{-}R_4\text{-}T)$ is removed." P_{Hc1} is C (cysteine); therefore in the formula of $P_{Hc1} = A_c(A_H)_nA_m$, A_c = cysteine, A_m = covalent bond, and since n = 0 A_H is 0. P_{Hc2} is K (lysine); therefore in the formula of $P_{Hc2} = A_m(A_H)_nA_c$, A_c = carboxylic acid moieties since y = 0, A_m = covalent bond, and since n = 0, A_H is 0. P_s is EEEFIYGAFKKK (SEQ. ID. No. 1).

5. Claims 42-43, 45-48, 58, 61, 63, 67-70, 72-77 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to ***nonelected species***, there being no allowable generic or linking claim. Election was made **without** traverse in Paper filed 3/12/04.

Information Disclosure Statement

6. The information disclosure statements (IDS) submitted by applicant filed on 5/2/01 (Paper No. 3), 6/6/02 (Paper No. 9), and 3/25/03 (Paper No. 13) are acknowledged and considered as noted on PTO-1449.

7. Claims 41, 44, 49-52, 54-57, 59-60, 62, 64-66, and 71 are treated on the merit in this Office Action.

8. Please note: Applicant's *specifically* elected species that is Texas Red-Jeffamine$_{900}$-CEEEFIYGAFKKKK [SEQ. ID. No. 1](see specification page 34, scheme 2; also paragraph 4 above) was searched and was not found in the prior art. Also, see MPEP § 803.02 (emphasis added):

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

Thus the search was expanded to non-elected species, which *were* found in the prior art, see rejections below.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 41, 49-52, 54-57, 59-60, and 71 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacobs et al. (US Patent 5,853,723).

Jacobs et al. disclose a library of peptidic substrates (col. 12, lines 45-55). The peptidic substrate comprises an antibody (peptide (P_s)) coupled to polyethylene glycol (PEG) that is labeled with fluorescein isothiocyanate (*F; refers to claims 49-51) (col. 9, lines 13-24; col. 12, lines 45-62; col. 13, line 65 to col. 14, line 12; fig. 2). The peptidic substrates of Jacobs et al. read on the claimed substrate member with the general formula of *F-R_1-L_1-R_2-P_{Hc1}-P_S-P_{Hc2}-(R_3-L_2-R_4-T)$_y$, wherein y is 0 (refers to claims 41 and 71), both P_{Hc1} and P_{Hc2} are covalent bond (refers to claims 41 and 60), L_1 is polyethylene glycol (PEG) (refers to claims 41 and 52), R_1 is a covalent bond consisting of a sulfur heteroatom (refers to claim 41), and R_2 is a thioether covalent linkage (refers to claims 41 and 59) (fig. 2). The polyethylene glycol has molecular weight ranging from 200 to 8,000 (col. 6, lines 11-15; col. 7, lines 48-57; col. 12, lines 63-67). Therefore, the library of Jacobs et al. anticipates the presently claimed library.

11. Claims 41, 44, 49-52, 60, 64-66, and 71 are rejected under 35 U.S.C. 102(b) as being anticipated by Burbaum et al. (US Patent 5,876,946).

Burbaum et al. disclose a library of peptidic substrates (col. 14, line 59 to col. 15, line 11). The peptidic substrate comprises a peptide (P_s) with a kinase domain affixed to a polymer bead and labeled with Cy5 (*F; refers to claims 49-51). The peptide comprises "end" residues (P_{Hc1} and P_{Hc2}) with different net charged (col. 14, lines 62-63) (refers to claims 64-66). The polymer bead includes polyethylene glycol (PEG)-grafted polystyrene bead (col. 6, lines 44-61). The label includes other fluorescent label such as Texas red and chemiluminescent label (col. 4, lines 31-41; col. 8, lines 62-65). The peptidic substrates of Burbaum et al. read on the claimed substrate member with the general formula of *F-R_1-L_1-R_2-P_{Hc1}-P_S-P_{Hc2}-(R_3-L_2-R_4-T)$_y$, wherein y is 0 (refers to claims 41 and 71), L_1 is polyethylene glycol (PEG) (refers to claims 41 and 52), R_1 is a covalent bond consisting of a nitrogen heteroatom (refers to claim 41), and R_2 is a covalent bond consisting of an oxygen heteroatom (refers to claim 41). Thus the library of Burbaum et al. anticipates the presently claimed library.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 41, 44, 49-52, 54-57, 59-60, 62, 64-66, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacobs et al. (US Patent 5,853,723) and Pomroy et al. (*Biochemical and Biophysical Research Communications*, **1998**, 245(2): 618-621).

Jacobs et al. disclose a library of peptidic substrates (col. 12, lines 45-55). The peptidic substrate comprises an antibody (peptide (P_s)) coupled to polyethylene glycol (PEG) that is labeled with fluorescein isothiocyanate (*F; refers to claims 49-51) (col. 9, lines 13-24; col. 12, lines 45-62; col. 13, line 65 to col. 14, line 12; fig. 2). The peptidic substrates of Jacobs et al. read on the claimed substrate member with the general formula of *F-R_1-L_1-R_2-P_{Hc1}-P_S-P_{Hc2}-(R_3-L_2-R_4-T)$_y$, wherein y is 0 (refers to claims 41 and 71), both P_{Hc1} and P_{Hc2} are covalent bond (refers to claims 41 and 60), L_1 is polyethylene glycol (PEG) (refers to claims 41 and 52), R_1 is a covalent bond consisting of a sulfur heteroatom (refers to claim 41), and R_2 is a thioether covalent linkage (refers to claims 41 and 59) (fig. 2). The polyethylene glycol has molecular weight ranging from 200 to 8,000 (col. 6, lines 11-15; col. 7, lines 48-57; col. 12, lines 63-67).

The library of Jacobs et al. does not expressly include coupling the peptide to the polyethylene glycol (PEG) by way of the cysteine of the peptidic portion and the "end" residues (P_{Hc1} and P_{Hc2}) of the peptide has a different net charged.

Pomroy et al. disclose hydrophobic peptides wherein the peptide is coupled to the polyethylene glycol (PEG) by way of the cysteine with a PEG-a-cys reagent (Abstract; pg. 619, left col., line 60 to right col., line 2; fig. 2) (refers to claims 41, 44, and 59). The peptide comprises "end" residues (P_{Hc1} and P_{Hc2}) with different net charged (pg. 619, right col., lines 53-55) (refers to claims 64-66). There are several advantages for attaching Cys side chain to a thiol-reactive PEGs: 1) it can perform under mild reaction conditions allowing for the PEGylation of a target protein under non-denaturing conditions; 2) it is highly targeted; and the disulfide bond between the thiol-reactive Peg and the protein is cleavable with suitable disulfide-reducing agents (pg. 619, right col., lines 29-40).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include coupling the peptide to the polyethylene glycol (PEG) by way of the cysteine of the peptidic portion and the "end" residues (P_{Hc1} and P_{Hc2}) of the peptide has a different net charged as taught by Pomroy et al. in the library of Jacobs et al. One of ordinary skill in the art would have been motivated to include coupling the peptide to the polyethylene glycol (PEG) by way of the cysteine of the peptidic portion and the "end" residues (P_{Hc1} and P_{Hc2}) of the peptide has a different net charged in the library of Jacobs et al. for the advantage of providing a PEG reagents that can perform under mild reaction conditions allowing for the PEGylation of a target protein under non-denaturing conditions (Pomroy: pg. 619, right col., lines 29-40) since both Jacobs et al. and Pomroy et al. disclose composition wherein the peptide is coupled to the polyethylene glycol (Jacobs: col. 9, lines 13-24; Pomroy: pg. 618, right col., lines 18-33). Furthermore, one of ordinary skill in the art would have reasonably expectation of

success in the combination of Jacobs et al. and Pomroy et al. because Pomroy et al. disclose the success of PEGylation of the peptide using PEG-a-Cys reagent (pg. 620, lines 5-32; fig. 2).

15. Claims 41, 49-52, 54-57, 59-60, 62, 64-66, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lam et al. (*Int. J. Peptide Protein Res.*, **1995**, 45(6): 587-592) and Jacobs et al. (US Patent 5,853,723).

Lam et al. disclose a random peptide library comprise heptapeptide (P_s) affixed to a polyethylene glycol (PEG)-grafted polystyrene bead (pg. 588, left col., lines 3-9). The heptapeptide comprises "end" residues (P_{Hc1} and P_{Hc2}) with different net charged (pg. 589, left col., lines 45-57) (refers to claims 64-66). The peptide library is labeled with a radioactive label (pg. 588, left col., lines 52-56; pg. 589, lines 45-57).

The library of Lam et al. does not expressly disclose optically labeling the library.

Jacobs et al. disclose a library of peptidic substrates (col. 12, lines 45-55). The peptidic substrate comprises an antibody (peptide (P_s)) coupled to polyethylene glycol (PEG) that is labeled with fluorescein isothiocyanate (*F; refers to claims 49-51) (col. 9, lines 13-24; col. 12, lines 45-62; col. 13, line 65 to col. 14, line 12; fig. 2). The peptidic substrates of Jacobs et al. read on the claimed substrate member with the general formula of *F-R_1-L_1-R_2-P_{Hc1}-P_S-P_{Hc2}-(R_3-L_2-R_4-T)$_y$, wherein y is 0 (refers to claims 41 and 71), both P_{Hc1} and P_{Hc2} are covalent bond (refers to claims 41 and 60), L_1 is polyethylene glycol (PEG) (refers to claims 41 and 52), R_1 is a covalent bond consisting of a sulfur heteroatom (refers to claim 41), and R_2 is a thioether covalent linkage (refers to claims 41 and 59) (fig. 2). The polyethylene glycol has molecular weight ranging from 200 to 8,000 (col. 6, lines 11-15; col. 7, lines 48-57; col. 12, lines 63-67).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include optically labeling the library as taught by Jacobs et al. in the library of Lam et al. One of ordinary skill in the art would have been motivated to include optically labeling the library in the library of Lam et al. because the type of label use would be a choice of experimental design and is considered within the purview of the cited prior art. Additionally, both Lam et al. and Jacobs et al. disclose the library of peptidic substrates comprise a peptide affixed to a polymer wherein the polymer include polyethylene glycol (PEG) (Jacobs: col. 9, lines 13-24; Lam:). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Lam et al. and Jacobs et al. because Jacobs et al. disclose that the peptidic substrates can be labeled with either a radioactive label or a fluorescent label (col. 13, lines 16-19). Thus the type of label use would be considered a choice of experimental design.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
June 3, 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER